Synthesis of Furoxans from Styrenes under Basic or Neutral Conditions

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Abstract: Furoxans (1,2,5-oxadiazole 2-oxides) can be synthesized from the corresponding styrenes using NOBF₄ under basic or even almost neutral reaction conditions. Acid-sensitive functional groups are tolerated under the developed basic conditions. For the substrates having poor reactivity, almost neutral conditions (using pyridine equimolar to NOBF₄) are suitable for better yields.

Key words: heterocycles, nitrogen-containing compounds, furoxans, styrenes, cyclization

Furoxans (1,2,5-oxadiazole 2-oxides) have a unique molecular structure and have been studied by many scientists with regard to their structure, chemical properties and synthesis.¹ Additionally, since furoxan derivatives have been found to activate a soluble guanylate cyclase by evolving nitric oxide (NO), attention has been paid to the potency of furoxans as a novel type of drug.² Pioneered by Gasco and co-workers, hybrid drugs, which contain a furoxan ring and a pharmacologically active molecular structure in one molecule, have been developed.³

Several synthetic methods for furoxans are known, such as dehydration of α -nitro oximes,⁴ dimerization of nitrile *N*-oxides⁵ and oxidation of α -dioximes.⁶ The most direct way to a furoxan bearing two different substituents is considered to be the reaction of an alkene with N₂O₃, since many alkenes are commercially available (chemical feedstock) and readily prepared. However, the only reported conditions for synthesizing furoxans from alkenes involve the treatment of alkenes with NaNO₂ (aqueous solution or neat) in glacial acetic acid, typically at below room temperature.⁷ The reported chemical yields are usually low to moderate and the substrate scope is rather limited. For further study on furoxan-based drug discovery, such as structure-activity relationships, the development of alternative synthetic methods for furoxans is highly required. Accordingly, we sought out such a method and have found that furoxans can be obtained from the corresponding styrenes using NOBF₄ under basic or almost neutral reaction conditions.

For the initial investigation, β -methylstyrene (1a) and NOBF₄, as an alkene substrate and a nitrosyl source, respectively, were used (Table 1). While trialkylamines were revealed as an unsuitable choice of solvent in this transformation (Table 1, entries 1 and 2), the use of pyridine as a solvent provided the desired furoxan in good

SYNTHESIS 2013, 45, 1524–1528 Advanced online publication: 14.05.2013 DOI: 10.1055/s-0033-1338436; Art ID: SS-2013-F0183-OP © Georg Thieme Verlag Stuttgart · New York yield (Table 1, entry 4). The fact that no product was obtained when a catalytic amount of pyridine and a solvent amount of triethylamine were used (Table 1, entry 5) may suggest that the trialkylamine strongly interacts with NOBF₄ and decomposes or deactivates it. It is of note that, though reaction time was compromised, decreasing the amount of pyridine from a solvent amount to equimolar to NOBF₄ did not affect the chemical yield (Table 1, entry 8), meaning that a furoxan can be synthesized from an alkene under almost neutral conditions.

Table 1 Optimization of the Reaction Conditions for Furoxan Synthesis from $\beta\text{-Methylstyrene}^a$

	NOBF ₄ (3 equiv) base solvent, 0 °C	-0- +	*_O_N	
((1	E)-1a mmol) 2aA		2aB	
Entry	Solvent + base	Time (h)	Yield (%)	
1	Et ₃ N (3 mL)	48	0	
2	DIPEA (3 mL)	72	0	
3	2,6-lutidine (3 mL)	72	21	
4	pyridine (3 mL)	0.2	65	
5	Et ₃ N (3 mL) + pyridine (0.1 equiv)	48	0	
6	THF (3 mL) + pyridine (3 equiv)	48	0	
7	MeCN (3 mL) + pyridine (3 equiv)	4	27	
8	CH_2Cl_2 (3 mL) + pyridine (3 equiv)	4	69	

^a The regioselectivity (**2aA/2aB**) was within the range of 87:13 to 96:4 in all cases where the products were obtained.

With the optimized conditions (Table 1, entry 4 or 8) in hand, several styrene derivatives were employed to investigate the substrate scope (Table 2).⁸ *cis*- β -Methylstyrene was converted under the optimized conditions into the corresponding furoxan **2a** in almost the same yield and selectivity as that of *trans*- β -methylstyrene (Table 2, entries 1 and 2). Similarly, both *trans*- and *cis*-stilbene gave the corresponding furoxan **2b** (Table 2, entries 3 and 4). The product yield (42%) is better than that obtained under the conventional acidic conditions (26%).⁹ The substrates bearing a long alkyl chain (Table 2, entries 5 and 6), a free hydroxy group (Table 2, entry 7) and various substituents on the aromatic ring (Table 2, entries 8–10) successfully

reacted with NOBF₄ to afford the furoxans in moderate to good yields with good regioselectivity. It seems that a substrate with a strong electron-donating group, such as a methoxy group on an aromatic ring, produces byproducts derived from oxidation of the aromatic ring by NOBF₄, and a lower yield of furoxan was obtained (Table 2, entry 9). A secondary alkyl substituent at the β -position was also tolerated (Table 2, entry 11). To our delight, relatively acid-sensitive protecting groups, namely O-tetrahydropyranyl (THP) and O-tert-butyldimethylsilyl (TBS), survived under our basic reaction conditions and the corresponding furoxans 2j and 2k were successfully obtained in good yields (Table 2, entries 12 and 13). An alkene in a cyclic system reacted with NOBF4 to provide the corresponding furoxan 21 with excellent selectivity (Table 2, entry 14). Ethyl cinnamate provided the furoxan 2m in very low yield (6%) under the basic conditions (3 equiv of NOBF₄ in pyridine solvent). This is presumably because an electron-deficient olefin such as ethyl cinnamate reacts poorly with NOBF₄, and during the reaction NOBF₄ gradually decomposes by mediation of the excess amount of pyridine.¹⁰ This problem could be overcome by reducing the amount of pyridine (the reaction conditions of entry 8 in Table 1), and a 49% yield of furoxan 2m was obtained (Table 2, entry 15). These almost neutral conditions (3) equiv of NOBF₄ and 3 equiv of pyridine in CH_2Cl_2) are seemingly suitable for substrates having poor reactivity.

 Table 2
 Furoxan Synthesis from Styrenes under Basic or Almost

 Neutral Conditions^a
 Particular

Ar	R	NOBF ₄ (3 equiv)	Ar A	0,+,0 + // Ar	N K R
Entry	Subst	rate	Product	Yield ^b (%)	A/B^{c}
1			2a	65	87:13
2			2a	57	95:5
3 ^d		Ph	2b	42	_
4		Ph	2b	33	_
5		C ₅ H ₁₁	2c	75	88:12
6		C ₅ H ₁₁	2d	68	96:4
7 ^d		ОН	2e	47	92:8

 Table 2
 Furoxan Synthesis from Styrenes under Basic or Almost

 Neutral Conditions^a (continued)
 Particular

Ar	NOBF₄ (3 equiv) pyridine, 0 °C	Ar A	0,+,C + Ar	N // R
Entry	Substrate	Product	Yield ^b (%)	A/B ^c
8	Br C5H11	2f	78	95:5
9	MeO MeO	2g	20	91:9
10	0 ₂ N	2h	67	90:10
11		2i	56	85:15
12	ОТНР	2ј	53	91:9
13	OTBS	2k	69	87:13
14		21	58	>95:5
15 ^e	CO ₂ Et	2m	49	>95:5

^a To a solution of a styrene (1 mmol) in pyridine (3 mL) was added NOBF_4 (3 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 0.2–48 h. Where indicated, a *trans/cis* mixture of starting styrene was used (see experimental section for details).

^b Isolated yield.

^c Determined by ¹H NMR spectroscopy of the crude material.

^d NOBF₄ (6 equiv) was used.

 $^{\rm e}$ To a solution of styrene (1 mmol) and pyridine (3 mmol) in CH_2Cl_2 (3 mL) was added NOBF_4 (3 mmol) at 0 °C.

In all the reactions conducted, the major regioisomer was found to be the furoxan **A** bearing the external oxygen atom on the nitrogen distal from the aromatic ring. The structures of the major regioisomer of **2a** and **2l** were unambiguously determined by X-ray diffraction analyses (Figure 1).¹¹ The structures of the other products, except **2m**, were assigned on the basis of the knowledge that the *N*-oxide group exerts a shielding influence on the ¹H resonance of the adjacent aliphatic substituent.^{12,13} As for compound **2m**, its structure could be determined after conversion of **2m** into **2e** and comparison by ¹H NMR spectroscopy (Scheme 1).



Figure 1 Representation of the crystal structures of 2a (top) and 2l (bottom)



Scheme 1 Sodium borohydride reduction of 2m to 2e

In summary, we have found that furoxans can be synthesized from the corresponding styrenes using NOBF₄ under basic or even almost neutral reaction conditions. Acidsensitive functional groups are tolerated under the developed basic conditions. For the substrates having poor reactivity, almost neutral conditions (using pyridine equimolar to NOBF₄) are suitable for better yields. Investigations to reveal the reaction mechanism and the origin of the regioselectivity are now ongoing in our laboratory.¹⁴

All reactions were carried out in well-cleaned and oven-dried glassware with magnetic stirring. Operations were performed under an atmosphere of dry argon using Schlenk and vacuum techniques. All starting materials were obtained from commercial sources or were synthesized using standard procedures. Melting points were measured on a Yanaco MP-500D apparatus and are not corrected. ¹H and ¹³C NMR spectra (400 and 100 MHz, respectively) were recorded on a JEOL JNM-LA 400 instrument using TMS (0 ppm) and CDCl₃ (77.0 ppm) as an internal standard, respectively. Mass spectra were measured using a Thermo Quest LCQ DECA plus spectrometer. Elemental analyses were carried out using a Yanako CHN Corder MT-5 instrument. Preparative column chromatography was performed using Fuji Silysia BW-4:10MH silica gel or YMC_Gel Silica (6 nm I-40–63 μ m). Thin-layer chromatography (TLC) was carried out on Merk 25 TLC silica gel 60 F₂₅₄ aluminum sheets. The identity of the following known compounds was confirmed by a comparison of the ¹H and ¹³C NMR spectra with the previously reported data: 3-methyl-4-phenylfuroxan (**2a**), ¹⁵ 3,4-diphenylfuroxan (**2b**),⁹ 3-(hydroxymethyl)-4-phenylfuroxan (**2e**).^{7b}

Furoxans from Styrenes and ${\bf NOBF}_4$ in Pyridine Solvent; General Procedure

To a stirred soln of a styrene (1 mmol) in pyridine (3 mL) was added NOBF₄ (3 mmol) at 0 °C. Stirring was continued at 0 °C for the indicated period and then the solution, diluted with H₂O (20 mL), was extracted with H₂O (3 × 20 mL). The combined organic layer was washed with H₂O (20 mL) and dried (Na₂SO₄). The residue obtained after evaporation of the volatiles was purified by chromatography on silica gel (EtOAc–hexane) to give the product as an inseparable mixture of regioisomers.

3-Methyl-4-phenylfuroxan (2a)¹⁵

Colorless needles; yield: 116 mg (65%) from the reaction (10 min) using the *trans*-alkene; yield: 101 mg (57%) from the reaction (10 min) using the *cis*-alkene.

 $R_f = 0.35$ (hexane-EtOAc, 10:1).

IR (neat): 1157, 1184, 1202, 1330, 1390, 1429, 1448, 1465, 1574, 1592, 2922 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ (**2aA**) = 2.37 (s, 3 H, Ar-*CH*₃), 7.54–7.58 (m, 3 H, Ar-*H*), 7.68 (m, 2 H, Ar-*H*); δ (**2aB**, distinguishable peak) = 2.55 (s, 3 H, Ar-*CH*₃).

¹³C NMR (100 MHz, CDCl₃): δ (**2aA**) = 156.8, 131.0, 129.2, 127.3, 126.6, 112.1, 9.2.

3,4-Diphenylfuroxan (2b)⁹

Colorless needles; yield: 99 mg (42%) from the reaction (1 h) using the *trans*-alkene; yield: 80 mg (33%) from the reaction (2 d) using the *cis*-alkene.

 $R_f = 0.4$ (hexane–EtOAc, 10:1).

IR (neat): 1327, 1419, 1441, 1503, 1572, 1590, 3026 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.43–7.53 (m, 10 H, Ar-*H*).

¹³C NMR (100 MHz, CDCl₃): δ = 156.2, 131.0, 130.5, 129.0, 128.9, 128.6, 128.2, 126.6, 122.8.

MS (EI): $m/z = 238 [M]^+$, 178 $[M - 60]^+$.

3-Pentyl-4-phenylfuroxan (2c)

Yellow oil; yield: 175 mg ($\hat{75\%}$) from the reaction (5 h) using the geometric mixture of alkenes (*cis/trans* = 67:33).

 $R_f = 0.35$ (hexane–EtOAc, 10:1).

IR (neat): 670, 768, 1418, 1455, 1576, 1593, 1572, 2860, 2929, 2957 $\rm cm^{-1}.$

¹H NMR (400 MHz, CDCl₃): δ (**2cA**) = 0.86 (t, *J* = 6.8 Hz, 3 H, CH₂CH₂CH₃), 1.29–1.35 (m, 4 H, CH₂CH₂CH₃), 1.61–1.65 (m, 2 H, CH₂CH₂CH₂CH₃), 2.71 (t, *J* = 7.2 Hz, 2 H, Ar-CH₂), 7.50–7.58 (m, 3 H, Ar-H), 7.64–7.71 (m, 2 H, Ar-H); δ (**2cB**, distinguishable peak) = 2.84 (t, *J* = 7.6 Hz, 2 H, Ar-CH₂).

¹³C NMR (100 MHz, CDCl₃): δ (**2cA**) = 156.8, 130.9, 129.2, 127.3, 126.8, 123.1, 31.0, 25.0, 22.8, 22.0, 13.7; δ (**2cB**, distinguishable peaks) = 157.2, 130.3, 129.1, 127.5, 26.6, 25.9.

MS (EI): $m/z = 232 [M]^+$, 172 $[M - 60]^+$.

Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.17; H, 7.04; N, 11.92.

4-(2-Naphthyl)-3-pentylfuroxan (2d)

Yellow oil; yield: 191 mg (68%) from the reaction (0.5 h) using the geometric mixture of alkenes (*cis/trans* = 70:30).

 $R_f = 0.32$ (hexane-EtOAc, 10:1).

IR (neat): 750, 818, 1418, 1461, 1590, 2859, 2928, 2955 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ (**2dA**) = 0.86 (t, J = 7.2 Hz, 3 H, CH₂CH₂CH₂CH₃), 1.26–1.38 (m, 6 H, CH₂CH₂CH₂CH₃), 2.80 (t, J = 8.0 Hz, 2 H, Ar-CH₂), 7.57–7.64 (m, 2 H, Ar-H), 7.75 (dd, J = 1.2, 7.2 Hz, 1 H, Ar-H), 7.91–8.02 (m, 3 H, Ar-H), 8.13 (s, 1 H, Ar-H); δ (**2dB**; distinguishable peak) = 2.92 (t, J = 8.0 Hz, 2 H, Ar-CH₂).

¹³C NMR (100 MHz, CDCl₃): δ (**2dA**) = 156.9, 134.1, 132.9, 129.3, 128.6, 128.0, 127.8, 127.7, 127.2, 124.2, 123.9, 115.8, 31.6, 25.5, 23.6, 22.5, 14.2; δ (**2dB**; distinguishable peaks) = 26.8, 26.0.

MS (EI): $m/z = 282 [M]^+, 222 [M - 60]^+$.

Anal. Calcd for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.43; N, 9.92. Found: C, 72.26; H, 6.54; N, 9.78.

3-(Hydroxymethyl)-4-phenylfuroxan (2e)7b

White solid; yield: 91 mg (47%) from the reaction (1 h) using the *trans*-alkene.

 $R_f = 0.6$ (hexane–EtOAc, 1:1).

IR (neat): 1010, 1409, 1462, 1575, 1599, 2930, 3402 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ (**2eA**) = 2.48 (s, 1 H, OH), 4.76 (s, 2 H, CH₂), 7.51–7.60 (m, 3 H, Ar-*H*), 7.80–7.83 (m, 2 H, Ar-*H*); δ (**2eB**; distinguishable peak) = 4.89 (s, 2 H, CH₂).

¹³C NMR (100 MHz, CDCl₃): δ (**2eA**) = 156.8, 131.4, 129.4, 127.7, 126.1, 53.3; δ (**2eB**; distinguishable peaks) = 130.7, 129.2, 127.4, 56.6.

MS (EI): $m/z = 192 [M]^+$, $132 [M - 60]^+$.

4-(3-Bromophenyl)-3-pentylfuroxan (2f)

Yellow oil; yield: 240 mg (78%) from the reaction (1.5 h) using the geometric mixture of alkenes (*cis/trans* = 84:16).

 $R_f = 0.25$ (hexane-EtOAc, 10:1).

IR (neat): 1429, 1455, 1564, 1593, 2859, 2929, 2956 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ (**2fA**) = 0.85–0.91 (m, 3 H, CH₂CH₂CH₃), 1.29–1.36 (m, 4 H, CH₂CH₂CH₃), 1.61–1.67 (m, 2 H, CH₂CH₂CH₂CH₂CH₃), 2.69 (t, *J* = 8.4 Hz, 2 H, Ar-CH₂), 7.41 (t, *J* = 8.4 Hz, 1 H, Ar-H), 7.58 (dt, *J* = 1.2, 7.6 Hz, 1 H, Ar-H), 7.69 (dt, *J* = 0.8, 8.0 Hz, 1 H, Ar-H), 7.83 (t, *J* = 1.6 Hz, 1 H, Ar-H); δ (**2fB**; distinguishable peak) = 2.83 (t, *J* = 7.6 Hz, 2 H, Ar-CH₂).

¹³C NMR (100 MHz, CDCl₃): δ (**2fA**) = 155.6, 134.0, 130.8, 130.5, 128.8, 126.0, 123.3, 115.4, 31.1, 25.1, 22.9, 22.0, 13.8; δ (**2fB**; distinguishable peaks) = 133.5, 130.6, 130.4, 126.1, 26.7, 25.9, 22.1, 13.8.

MS (EI): $m/z = 251.1 [M - 60]^+$.

Anal. Calcd for $C_{13}H_{15}BrN_2O_2:$ C, 50.18; H, 4.86; N, 9.00. Found: C, 50.31; H, 4.86; N, 9.05.

4-(4-Methoxyphenyl)-3-pentylfuroxan (2g)

Yellow oil; yield: 52 mg (20%) from the reaction (0.5 h) using the geometric mixture of alkenes (*cis/trans* = 55:45).

 $R_f = 0.25$ (hexane-EtOAc, 10:1).

IR (neat): 1175, 1253, 1435, 1450, 1574, 1592, 2860, 2930, 2957 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ (**2gA**) = 0.85–0.91 (m, 3 H, CH₂CH₂CH₃), 1.25–1.39 (m, 4 H, CH₂CH₂CH₃), 1.59–1.73 (m, 2 H, CH₂CH₂CH₂CH₂CH₃), 2.69 (t, *J* = 7.6 Hz, 2 H, Ar-CH₂), 3.87 (s, 3 H, Ar-OCH₃), 7.01–7.07 (m, 2 H, Ar-H), 7.65–7.68 (m, 2 H, Ar-H); δ (**2gB**; distinguishable peak) = 2.82 (t, *J* = 8 Hz, Ar-CH₂).

¹³C NMR (100 MHz, CDCl₃): δ (**2gA**) = 161.6, 156.5, 129.1, 119.1, 115.7, 114.7, 55.4, 31.2, 25.2, 23.1, 22.2, 13.8; δ (**2gB**; distinguishable peaks) = 128.9, 114.6, 22.1.

MS (EI): $m/z = 262.0 \text{ [M]}^+$, 202.1 [M - 60]⁺.

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Anal. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.11; H, 6.92; N, 10.68. Found: C, 64.19; H, 7.15; N, 10.07.

4-(4-Nitrophenyl)-3-pentylfuroxan (2h)

Pale yellow needles; yield: 185 mg ($\hat{67\%}$) from the reaction (48 h) using the geometric mixture of alkenes (*cis/trans* = 63:37).

 $R_f = 0.2$ (hexane–EtOAc, 5:1).

IR (neat): 713, 851, 1250, 1434, 1534, 1587, 2860, 2931, 2958 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ (**2hA**) = 0.85–0.91 (m, 3 H, CH₂CH₂CH₃), 1.25–1.39 (m, 4 H, CH₂CH₂CH₃), 1.59–1.73 (m, 2 H, CH₂CH₂CH₂CH₃), 2.74 (t, *J* = 8 Hz, 2 H, Ar-CH₂), 7.87–7.97 (m, 2 H, Ar-*H*), 7.99–8.44 (m, 2 H, Ar-*H*); δ (**2hB**; distinguishable peak) = 2.90 (t, *J* = 8 Hz, 2 H, Ar-CH₂).

¹³C NMR (100 MHz, CDCl₃): δ (**2hA**) = 155.0, 149.2, 132.9, 128.5, 124.5, 115.0, 31.2, 25.2, 23.0, 22.1, 13.7.

MS (EI): $m/z = 217 [M - 60]^+$.

Anal. Calcd for $C_{13}H_{15}N_3O_4$: C, 56.31; H, 5.45; N, 15.15. Found: C, 56.36; H, 5.45; N, 15.17.

3-Isopropyl-4-(2-naphthyl)furoxan (2i)

Colorless needles; yield: 144 mg (56%) from the reaction (2 h) using the geometric mixture of alkenes (*cis/trans* = 85:15).

 $R_f = 0.42$ (hexane–EtOAc, 10:1).

IR (neat): 754, 811, 864, 1324, 1385, 1202, 1420, 1455, 1591, 2937, 2982 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ (**2iA**) = 1.37 (d, *J* = 6.8 Hz, 6 H, 2 × CH₃), 3.21 (septet, *J* = 6.8 Hz, 1 H, CH), 7.55–7.69 (m, 3 H, Ar-*H*), 7.88–8.20 (m, 4 H, Ar-*H*); δ (**2iB**; distinguishable peak) = 3.30 (septet, *J* = 6.8 Hz, 1 H, CH).

¹³C NMR (100 MHz, CDCl₃): δ (**2iA**) = 157.0, 132.8, 129.1, 128.5, 128.4, 127.9, 127.8, 127.2, 124.6, 124.0, 118.7, 23.8, 17.1; δ (**2iB**; distinguishable peaks) = 162.2, 133.7, 132.9, 129.1, 128.5, 127.9, 127.8, 127.1, 124.1, 23.8, 17.1.

MS (EI): $m/z = 254 [M]^+$, 194 $[M - 60]^+$.

Anal. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.36; H, 5.56; N, 10.92.

4-Phenyl-3-[(tetrahydro-2*H*-pyran-2-yloxy)methyl]furoxan (2j)

Colorless oil; yield: 145.6 mg (53%) from the reaction (0.5 h) using the *trans*-alkene.

 $R_f = 0.35$ (hexane–EtOAc, 10:1).

IR (neat): 963, 1010, 1058, 1076, 1119, 1479, 1577, 1597, 2942 $\rm cm^{-1}.$

¹H NMR (400 MHz, CDCl₃): δ (**2jA**) = 1.51–1.81 (m, 6 H, CH₂CH₂CH₂CH₂O), 3.52–3.57 (m, 2 H, OCH₂CH₂), 3.78–3.84 (m, 1 H, OCHO), 4.60 (d, *J* = 12.8 Hz, 1 H, Ar-CH₂), 4.74 (d, *J* = 12.8 Hz, 1 H, Ar-CH₂), 7.30–7.58 (m, 3 H, Ar-H), 7.83–7.94 (m, 2 H, Ar-H); δ (**2jB**; distinguishable peak) = 7.94–7.96 (m, 2 H, Ar-H).

¹³C NMR (100 MHz, CDCl₃): δ (**2jA**) = 157.1, 131.2, 129.2, 127.5, 126.5, 122.6, 112.9, 99.2, 62.3, 57.2, 30.2, 25.1, 18.9; δ (**2jB**; distinguishable peaks) = 154.3, 130.9, 129.3, 127.9, 122.9, 98.3, 59.8.

MS (EI): $m/z = 175 [M - 101 (OTHP)]^+$.

Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 61.00; H, 5.88; N, 9.76.

3-[(tert-Butyldimethylsilyloxy)methyl]-4-phenylfuroxan (2k)

Colorless oil; yield: 212 mg (69%) from the reaction (0.5 h) using the *trans*-alkene.

 $R_f = 0.4$ (hexane–EtOAc, 10:1).

IR (neat): 1276, 1384, 1434, 1461, 1579, 1600, 2853, 2930, 2957 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ (**2kA**) = 0.14 (s, 6 H), 0.88 (s, 9 H), 4.72 (s, 2 H), 7.47–7.58 (m, 3 H, Ar-*H*), 7.91–7.94 (m, 2 H, Ar-*H*); δ (**2kB**; distinguishable peak) = 4.83 (s, 2 H).

¹³C NMR (100 MHz, CDCl₃): δ (**2kA**) = 157.5, 131.5, 129.1, 127.8, 126.6, 114.2, 54.1, 25.6, 18.1, -5.3; δ (**2kB**; distinguishable peaks) = 130.5, 129.0, 127.6, 57.1.

MS (EI): $m/z = 249 [M - 57 (t-Bu)]^+$, 189 $[M - 57 - 60]^+$.

Anal. Calcd for $C_{15}H_{22}N_2O_3Si:$ C, 58.79; H, 7.24; N, 9.14. Found: C, 58.70; H, 7.36; N, 9.20.

4,5-Dihydronaphtho[1,2-c][1,2,5]oxadiazole 3-Oxide (21)

White solid; yield: 103 mg (58%) from the reaction (1 h) using the cyclic alkene.

Mp 84.4-85.5 °C.

 $R_f = 0.3$ (hexane–EtOAc, 10:1).

IR (neat): 1350, 1434, 1535, 1587, 2861, 2959 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ (**2**IA) = 2.95 (t, *J* = 7.6 Hz, 2 H, Ar-CH₂CH₂CN), 3.12 (t, *J* = 7.6 Hz, 2 H, Ar-CH₂CH₂CN), 7.33–7.48 (m, 3 H, Ar-*H*), 7.98–8.00 (dd, *J* = 1.2, 9.2 Hz, 1 H, Ar-*H*).

¹³C NMR (100 MHz, CDCl₃): δ (**2IA**) = 153.4, 136.9, 131.6, 129.1, 127.8, 124.3, 123.6, 111.3, 27.2, 18.0.

MS (EI): $m/z = 188.1 \text{ [M]}^+$, $128.1 \text{ [M} - 60\text{]}^+$.

Anal. Calcd for $C_{10}H_8N_2O_2$: C, 63.83; H, 4.29; N, 14.89. Found: C, 63.75; H, 4.30; N, 14.74.

Ethyl 4-Phenylfuroxan-3-carboxylate (2m)

Colorless oil; yield: 115 mg (49%) from the reaction (2 d) using the *trans*-alkene.

 $R_f = 0.35$ (hexane–EtOAc, 1:1).

IR (neat): 1184, 1202, 1330, 1390, 1429, 1448, 1465, 1478, 1574, 1592, 1734, 2979 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ (**2mA**) = 1.29 (t, *J* = 7.0 Hz, 3 H, OCH₂CH₃), 4.35–4.40 (q, *J* = 7.0 Hz, 2 H, OCH₂CH₃), 7.49–7.59 (m, 3 H, Ar-*H*), 7.64–7.71 (m, 2 H, Ar-*H*); δ (**2mB**; distinguishable peaks) = 1.39 (t, *J* = 7.0 Hz, 3 H, OCH₂CH₃), 4.46 (q, *J* = 7.0 Hz, 2 H, OCH₂CH₃).

¹³C NMR (100 MHz, CDCl₃): δ (**2mA**) = 156.5, 156.1, 131.6, 129.0, 128.5, 126.0, 63.0, 13.8; δ (**2mB**; distinguishable peaks) = 128.6, 128.4, 62.6.

MS (EI): $m/z = 234 [M]^+$, 174 $[M - 60]^+$.

Anal. Calcd for $C_{11}H_{10}N_2O_4{:}$ C, 56.41; H, 4.30; N, 11.96. Found: C, 56.52; H, 4.29; N, 11.80.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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